DIPHTHERIA

DISEASE REPORTING

In Washington

The last case of toxigenic diphtheria reported in Washington occurred in 1979. Cases are most often associated with travel as diphtheria is not endemic to Washington.

Purpose of reporting and surveillance

- To alert public health authorities to the presence of *C. diphtheria* and the possibility of other cases developing in the area, a particular concern given the large number of susceptible adults.
- To assist in the diagnosis of cases.
- To assure early and appropriate treatment with diphtheria antitoxin and antibiotics.
- To obtain necessary laboratory specimens before antibiotic or antitoxin treatment.
- To identify and evaluate contacts and recommend appropriate antibiotic prophylaxis to prevent further spread of the disease.

Reporting requirements

- Health care providers: **immediately notifiable to Local Health Jurisdiction**
- Hospitals: **immediately notifiable to Local Health Jurisdiction**
- Laboratories: notifiable to Local Health Jurisdiction within 2 workdays, specimen submission required
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

An upper-respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose.

Laboratory criteria for diagnosis

- Isolation of *Corynebacterium diphtheriae* from a clinical specimen or
- Histopathologic diagnosis of diphtheria.

Case definition

- Probable: a clinically compatible case that is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case.
- Confirmed: a clinically compatible case that is either laboratory confirmed or epidemiologically linked to a laboratory-confirmed case.
  Cutaneous diphtheria should not be reported. Respiratory disease caused by nontoxigenic C. diphtheriae should be reported as diphtheria. All diphtheria isolates, regardless of association with disease, should be sent to the Diphtheria Laboratory, National Center for Infectious Diseases, CDC.

A. DESCRIPTION

1. Identification

An acute bacterial disease that primarily involves the tonsils, pharynx, larynx, nose, occasionally other mucous membranes or skin and sometimes the conjunctivae or vagina. The characteristic lesion, caused by liberation of a specific cytotoxin, is an asymmetrical adherent grayish white membrane with surrounding inflammation. The throat is moderately to severely sore in faucial or pharyngotonsillar diphtheria, with cervical lymph nodes somewhat enlarged and tender; in moderate to severe cases, there is marked swelling and edema of the neck with extensive tracheal membranes that progress to airway obstruction.

Nasal diphtheria can be mild and chronic with one sided nasal discharge and excoriations. Inapparent infections (or colonization) outnumber clinical cases. The toxin can cause myocarditis, with heart block and progressive congestive failure beginning about 1 week after onset. Later effects include neuropathies that can mimic Guillain-Barre syndrome. Case-fatality rates of 5%-10% for noncutaneous diphtheria have changed little in 50 years. The lesions of cutaneous diphtheria are variable and may be indistinguishable from, or a component of, impetigo; peripheral effects of the toxin are usually not evident.

Diphtheria should be suspected in the differential diagnosis of bacterial (especially streptococcal) and viral pharyngitis, Vincent's angina, infectious mononucleosis, oral syphilis and candidiasis.

Presumptive diagnosis is based on observation of an asymmetrical, grayish white membrane, especially if it extends to the uvula and soft palate and is associated with tonsillitis, pharyngitis or cervical lymphadenopathy, or a serosanguinous nasal discharge. The diagnosis is confirmed by bacteriologic examination of lesions. If diphtheria is strongly suspected, specific treatment with antibiotics and antitoxin should be initiated while studies are pending and should be continued even in the face of a negative laboratory report.

2. Infectious Agent

Corynebacterium diphtheriae of gravis, mitis or intermedius biotype. Toxin production results when the bacteria are infected by corynebacteriophage containing the diphtheria

toxin gene tox. Nontoxigenic strains rarely produce local lesions; however, they have been increasingly associated with infective endocarditis.

3. Worldwide Occurrence

A disease of colder months in temperate zones, that primarily involves nonimmunized children under 15 years of age; often found among adults in population groups whose immunization was neglected. In the tropics, seasonal trends are less distinct; inapparent, cutaneous and wound diphtheria cases are much more common.

In the US, from 1980 to 1998, an average of fewer than 4 cases was reported annually; two thirds of the affected people were 20 years of age or older. A massive outbreak of diphtheria began in the Russian Federation in 1990 and spread to all countries of the former Soviet Union and Mongolia. Contributing factors included increased susceptibility among adults due to waning of vaccine induced immunity, failure to fully immunize children due to unwarranted contraindications, antivaccine movements and declining socioeconomic conditions. This epidemic began to decline after reaching a peak in 1995; however, it was responsible for more than 150,000 reported cases and 5,000 deaths between 1990-97. In Ecuador, an outbreak of diphtheria occurred in 1993-94, with about 200 cases, half of whom were 15 years of age or older. In both epidemics, control was achieved by mass immunization activities.

4. Reservoir

Humans.

5. Mode of Transmission

Contact with a patient or carrier; more rarely, contact with articles soiled with discharges from lesions of infected people. Raw milk has served as a vehicle.

6. Incubation period

Usually 2-5 days, occasionally longer.

7. Period of communicability

Variable, until virulent bacilli have disappeared from discharges and lesions; usually 2 weeks or less and seldom more than 4 weeks. Effective antibiotic therapy promptly terminates shedding. The rare chronic carrier may shed organisms for 6 months or more.

8. Susceptibility and resistance

Infants born of immune mothers are relatively immune; protection is passive and usually lost before the sixth month. Lifelong immunity is usually, but not always, acquired after disease or inapparent infection. Immunization with toxoid produces prolonged but not

lifelong immunity. Serosurveys in the US indicate that more than 40% of adults lack protective levels of circulating antitoxin; decreasing immunity levels have also been found in Canada, Australia and several European countries. However, many of these older adults may have immunologic memory and would be protected against disease after exposure. In the US, most children have been immunized; by the second quarter of 1997, 95% of 2 year old children had received 3 doses of diphtheria vaccine. Antitoxic immunity protects against systemic disease but not against colonization in the nasopharynx.

B. METHODS OF CONTROL

1. Preventive measures:

a. Educational measures are important: inform the public, and particularly the parents of young children, of the hazards of diphtheria and the necessity for active immunization.
b. The only effective control is widespread active immunization with diphtheria toxoid. Immunization should be initiated in infancy with a formulation containing diphtheria toxoid, tetanus toxoid and either acellular pertussis antigens (DtaP, the preferred preparation in the US) or whole cell pertussis vaccine (DTP). Formulations that combine diphtheria and tetanus toxoid, whole cell pertussis, and *Haemophilus influenzae* type b vaccine (DTP-Hib) are also available.
c. The following schedules are recommended for use in the US. (Some countries may recommend different ages for specific doses or fewer than 4 doses in the primary series.)
    i. For children less than 7 years of age—
    A primary series of diphtheria toxoid combined with other antigens, such as DTaP, or DTP-Hib. The first 3 doses are given at 4-to 8-week intervals beginning when the infant is 6-8 weeks old; a fourth dose is given 6-12 months after the third dose. This schedule does not need to be restarted because of any delay in administering the scheduled doses. A fifth dose is given at 4-6 years of age prior to school entry; this dose is not necessary if the fourth dose is given after the fourth birthday. If the pertussis component of DTP is contraindicated, diphtheria and tetanus toxoids for children (DT) should be substituted.
    ii. For persons 7 years of age and older—
    Because adverse reactions may increase with age, a preparation with a reduced concentration of diphtheria toxoid (adult Td) is usually used after the 7th birthday for booster doses. For a previously unimmunized individual, a primary series of 3 doses of adsorbed tetanus and diphtheria toxoids, Td, is given. The first 2 doses are given at 4-to 8-week intervals and the third dose 6 months to 1 year after the second dose. Limited data from Sweden suggest that this regimen may not induce protective antibody levels in most adults, and additional doses may be needed.
    iii. Active protection should be maintained by administering a dose of Td every 10 years thereafter.

d. Special efforts should be made to ensure that those who are at higher risk of patient exposure, such as health workers, are fully immunized and receive a booster dose of Td every 10 years.
e. For children and adults who are severely immunocompromised or infected with HIV, diphtheria immunization is indicated. Use the same schedule and dose as for immunocompetent persons, even though the immune response may be suboptimal.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Strict isolation for pharyngeal diphtheria, contact isolation for cutaneous diphtheria, until two cultures from both throat and nose (and skin lesions in cutaneous diphtheria), taken not less than 24 hours apart, and not less than 24 hours after cessation of antimicrobial therapy, fail to show diphtheria bacilli. Where culture is impractical, isolation may be ended after 14 days of appropriate antibiotic treatment (see B2g, below).
c. Concurrent disinfection: Of all articles in contact with patient and all articles soiled by discharges of patient. Terminal cleaning.
d. Quarantine: Adult contacts whose occupations involve handling food (especially milk) or close association with nonimmunized children should be excluded from that work until they have been treated as described below and bacteriologic examination proves them not to be carriers.
e. Management of contacts: All close contacts should have cultures taken from the nose and throat and should be kept under surveillance for 7 days. A single dose of benzathine penicillin (IM, see below for doses) or a 7-10 day course of erythromycin (PO) is recommended for all persons with household exposure to diphtheria, regardless of their immunization status. Those who handle food or work with school children should be excluded from work or school until bacteriologic examination proves them not to be carriers. Previously immunized contacts should receive a booster dose of diphtheria toxoid if more than 5 years have elapsed since their last dose, and a primary series should be initiated in nonimmunized contacts; use Td, DT, DTP, DTaP or DTP-Hib vaccine, depending on the contact's age.
f. Investigation of contacts and source of infection: The search for carriers by use of nose and throat cultures, other than among close contacts, is not ordinarily useful or indicated if provisions of B2e, above, are carried out.
g. Specific treatment: If diphtheria is strongly suspected on the basis of clinical findings, antitoxin (only antitoxin of equine origin is available) should be given immediately after bacteriologic specimens are taken, without waiting for results. Diphtheria antitoxin (DAT) is on the CDC Drug Service formulary as an investigational product. The National Immunization Program (NIP) responds to clinical inquiries for DAT during business hours (8:00 a.m. to 4:30 p.m. EST; Monday-Friday at 404-639-8255). After hours or on weekends and holidays, call the CDC Duty Officer at 404-639-2888. DAT is stored at quarantine stations around the country for rapid distribution. After completion of tests to rule out hypersensitivity, a single dose of 20,000-100,000 units is given IM, depending on the area of involvement and severity of the disease. Intramuscular administration usually suffices; in severe infections,

both IV and IM administration may be indicated. Antibiotics are not a substitute for antitoxin. Procaine penicillin G (IM) (25,000 to 50,000 units/kg/d for children and 1.2 million units/kg/d for adults, in 2 divided doses) or parenteral erythromycin (40-50 mg/kg/d, with a maximum of 2 g/d) has been recommended until the patient can swallow comfortably, at which point erythromycin PO in 4 divided doses or penicillin V PO (125-250 mg 4 times daily) may be substituted for a recommended total treatment period of 14 days. Some erythromycin resistant strains have been identified, but they are uncommon and not a public health problem. Newer macrolide antibiotics, including azythromycin and clarithromycin, should be effective for erythromycin susceptible strains, but these antibiotics do not offer any substantial advantage over erythromycin.

Prophylactic treatment of carriers: A single dose of benzathine penicillin G (IM) (600,000 units for persons less than 6 years of age and 1.2 million units for persons 6 years of age or older) or a 7-10 day course of erythromycin (PO) (40 mg/kg/d for children and 1 g/d for adults) has been recommended.

3. Epidemic measures

a. Immunize the largest possible proportion of the population group involved, emphasize protection of infants and preschool children. In an epidemic involving adults, immunize groups that are most affected and at high risk. Repeat immunization procedures 1 month later to provide at least 2 doses to recipients.
b. Identify close contacts and define population groups at special risk. In areas with appropriate facilities, carry out a prompt field investigation of reported cases to verify the diagnosis and to determine the biotype and toxigenicity of *C. diphtheriae*.

4. International measures

People traveling to or through countries where either faucial or cutaneous diphtheria is common should receive primary immunization if necessary, or a booster dose of Td for those previously immunized.